Pepper Hamilton LLP
Attorneys at Law

3000 Two Logan Square
Eighteenth and Arch Streets
Philadelphia, PA 19103-2799
215.981.4000
Fax 215.981.4750
www.pepperlaw.com

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(54) **DIPHENYLAZETIDINONE DERIVATIVES POSSESSING CHOLESTEROL ABSORPTION INHIBITORY ACTIVITY**

(75) Inventors: **Susanne Alenfalk**, Molndal (SE); **Mikael Dahlstrom**, Molndal (SE); **Fana Hunegnaw**, Molndal (SE); **Staffan Karlsson**, Molndal (SE); **Malin Lemurell**, Molndal (SE); **Ann-Margret Lindqvist**, Molndal (SE); **Tore Skjaret**, Molndal (SE); **Ingemar Starke**, Molndal (SE)

Correspondence Address:
Pepper Hamilton LLP
400 Berwyn Park, 899 Cassatt Road
Berwyn, PA 19312-1183

(73) Assignee: **ASTRAZENECA AB**, Sodertalje (SE)

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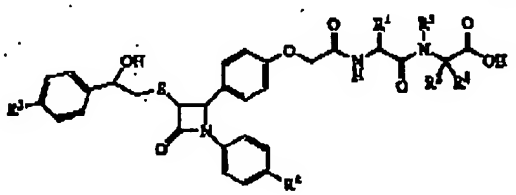
(57) **ABSTRACT**

Compounds of formula (I) (wherein variable groups are as defined within) pharmaceutically acceptable salts, solvates, solvates of such salts and prodrugs thereof and their use as cholesterol absorption inhibitors for the treatment of hyperlipidaemia are described. Processes for their manufacture and pharmaceutical compositions containing them are also described.

(I)



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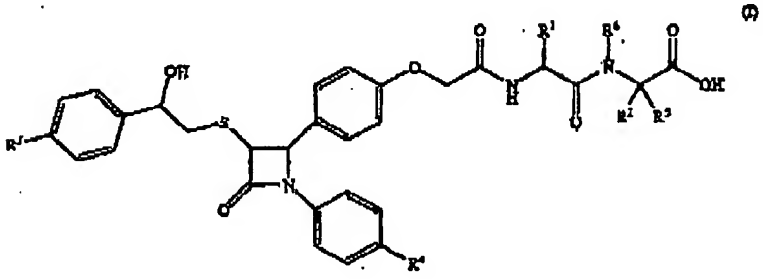
Compound (I)	Caco value (10^{-6} cm/sec)
N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-lysine	0.3
1-(4-Fluorophenyl)-3-(R)-[2-(4-fluorophenyl)-2-hydroxyethylthio]-4-(R)-{4-[N-{N-[2-(phenyl)-1-(R)-(carboxy)ethyl]carbamoylmethyl}carbamoylmethoxy]phenyl}azetidin-2-one	0.09

1. A compound of formula (I):



(I)

wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6}alkoxy, N—(C_{1-6}alkyl)amino, N,N-(C_{1-6}alkyl)$_2$amino, C_1-C_6 alkylcarbonylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^2 and R^3 are independently hydrogen, a branched or unbranched C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, $(C_1$-$C_6)_3$Si, N—(C_{1-6}alkyl)amino, (NAN-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkylS(O)$_a$, C_{3-6}cycloalkyl, aryl or aryl C_{1-6} alkylS(O)$_a$, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylR ;

R^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6}alkoxy;

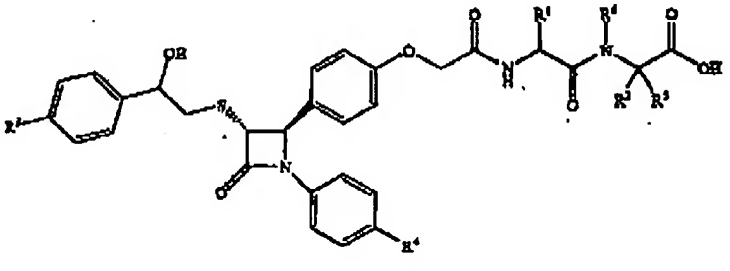
R^5 is hydrogen, C_{1-6} alkyl, or arylC$_{1-6}$ alkyl;

wherein R^3 and R^2 may form a ring with 2-7 carbon atoms and wherein R^5 and R^2 may form a ring with 3-6 carbon atoms;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(N-{N—[(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl}carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(N—{(R)-α-[N—[(S)-1-(carboxy)-2-(hydroxy)ethyl]carbamoyl}benzyl)carbamoylmethoxy]phenyl]azetidin-2-one.

2. A compound of formula (I2):



(I2)

wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6}alkoxy, N—(C_{1-6}alkyl)amino,

N,N-(C_{1-6}alkyl)$_2$amino, C_1-C_6 alkylcarbonylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^3 and R^5 are independently hydrogen, a branched or unbranched C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, $(C_1$-$C_6)_3Si$, N—(C_{1-6}alkyl)amino, N,N-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkylS(O)$_a$, C_{3-6}cycloalkyl, aryl or aryl C_{1-6}alkylS(O)$_a$, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6}alkylS—;

R^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6}alkoxy;

R^5 is hydrogen, C_{1-6} alkyl, or arylC$_{1-6}$ alkyl;

wherein R^3 and R^5 may form a ring with 2-7 carbon atoms and wherein R^4 and R^5 may form a ring with 3-6 carbon atoms;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(N-[N—{(R)-1-(carboxy)-2-(hydroxy)ethyl}carbamoylmethyl}carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-{4-[N-((R)-N-[(S)-1-(carboxy)-2-(hydroxy)ethyl]carbamoyl}benzyl)carbamoylmethoxy]phenyl}azetidin-2-one.

3. A compound according to claim 1, wherein:

R^1 is hydrogen or phenyl.

4. A compound according to claim 1, wherein:

R^2 is hydrogen, a branched or unbranched C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, acylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by hydroxy, alkyl, alkoxy or cyano.

5. A compound according to claim 1, wherein:

R^3 is hydrogen, C_1-C_6alkyl, halo or methoxy.

6. A compound according to claim 1, wherein:

R^3 is hydrogen, methyl, chlorine, fluorine, C_{1-6} alkylS , or methoxy.

7. A compound according to claim 1, wherein:

R^4 is hydrogen or halo.

8. A compound according to claim 1, wherein:

R^4 is chlorine or fluorine.

9. A compound according to claim 1, wherein:

R^5 is hydrogen, C_{1-6} alkyl, arylC$_{1-6}$alkyl or R^5 and R^5 form a ring with 3-6 carbon atoms.

10. A compound according to claim 1, wherein:

R^1 is hydrogen;

R^2 is a branched or unbranched C_{1-6}alkyl, optionally substituted by a C_{3-6}cycloalkyl, alkylS—, aryl optionally substituted by hydroxy or cyano, amino, N—(C_{1-6}alkyl)amino, N,N—(C_{1-6}alkyl)$_2$-amino or aryl C_{1-6} alkylS(O)$_a$, wherein a is 0-2;

R^3 and R^4 are halo;

R^5 is hydrogen or C_{1-6} alkyl; and

R^6 is hydrogen.

11. One or more compounds chosen from:

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-N^6-acetyl-D-lysine;

1-(4-Fluorophenyl)-3-(R)-[2-(4-fluorophenyl)-2-hydroxyethylthio]-4-(R)-{4-[N-{N-[2-(phenyl)-1-(R)-(carboxy)ethyl]carbamoylmethyl}carbamoylmethoxy]phenyl}azetidin-2-one;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-valine;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-tyrosine;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-proline;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-lysine;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-hydroxy-2-(4-methoxyphenyl)ethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-valine;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-2-butylnorleucine;

N-{[4-((2R,3R)-1-(4-Fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-S-methyl-L-cysteine;

N-{[4-((2R,3R)-1-(4-chlorophenyl)-3-{[2-(4-chlorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-cyclohexyl-D-alanine;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-cyclohexyl-D-alanine;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-4-methyl-L-leucine;

N-{[4-((2R,3R)-1-(4-Fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}-1-alanyl-D-valine;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-hydroxy-2-(4-methylphenyl)ethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-valine;

N-{[4-((2R,3R)-1-(4-chlorophenyl)-3-{[2-(4-chlorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-valine;

N-{[4-((2R,3R)-1-(4-chlorophenyl)-3-{[2-(4-chlorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-methyl-D-valine;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-(2-naphthyl)-D-alanine;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-methyl-D-valine;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-(3R,4S,5R)-3,4,5,6-tetrahydroxy-D-norleucine;

N-{[4-((2R,3R)-1-(4-Fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl glycyl-N,2 dimethylalanine;

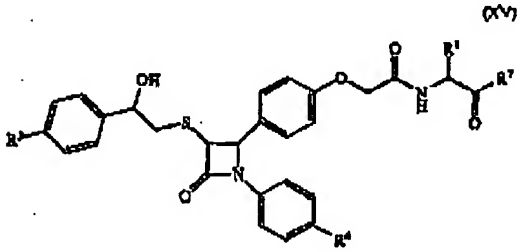
N-({4-[(2R,3R)-1-(4-Fluorophenyl)-3-{[2-hydroxy-2-(4-(methylthio)phenyl]ethyl}thio)-4-oxoazetidin-2-yl]phenoxy}acetyl)glycyl-3-methyl-D-valine-valine;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-S-(4-methylbenzyl)-D-cysteine;

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-S-(tert-butyl)-D-cysteine; and

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-b,b-dimethyl-D-phenylalanine.

12. A compound of the formula (XV) or hydrolysable esters or amides thereof:



(XV)

wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6}alkoxy, N—(C_{1-6}alkyl)amino, N,N—(C_{1-6}alkyl)$_2$amino, C_1-C_6 alkylcarboxy-lamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^2 and R^3 are independently hydrogen, a branched or unbranched C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, (C_1-C_6)$_3$Si, N—(C_{1-6}alkyl)amino, N,N—(C_{1-6}alkyl)$_2$amino, C_{1-6}alkylS(O)$_a$alkylC$_{1-6}$alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl, and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylS—;

R^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6}alkoxy;

R^6 is hydrogen, C_{1-6} alkyl, or arylC_{1-6} alkyl; and

R^7 is an hydroxy group or a C_{1-9} alkoxy group;

wherein R^2 and R^3 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(N-{N—[(R) — 1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl}carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-{4-[N—((R)-α-{N—[(S)-1-(carboxy)-2-(hydroxy)ethyl]carbamoyl}benzyl)carbamoylmethoxy]phenyl}azetidin-2-one.

13. A method of treating or preventing a hyperlipidemic condition comprising the administration of an effective amount of a compound according to claim 1 to a mammal in need thereof.

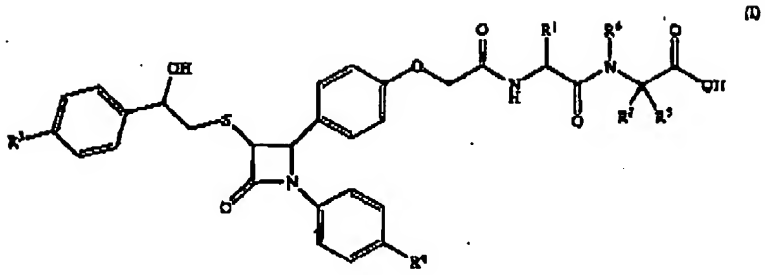
14. A method of treating or preventing atherosclerosis comprising the administration of an effective amount of a compound according to claim 1 to a mammal in need thereof.

15. A method for treating or preventing Alzheimers' disease comprising the administration of an effective amount of a compound according to claim 1 to a mammal in need thereof.

16. A method for treating or preventing a cholesterol associated tumor comprising the administration of an effective amount of a compound according to claim 1 to a mammal in need thereof.

17. A pharmaceutical formulation comprising a compound according to claim 1 in admixture with a pharmaceutically acceptable adjuvant, diluent and/or carrier.

18. A combination of a compound according to formula (I)



wherein:

R^1 is hydrogen, C_{1-6}alkyl C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6}alkoxy, N—(C_{1-6}alkyl)amino, N,N-(C_{1-6}alkyl)$_2$amino, C_1-C_6 alkylcarbonylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^2 and R^3 are independently hydrogen, a branched or unbranched C_{1-6}alkyl C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, $(C_1$-$C_6)_3$Si, N—(C_{1-6}alkyl)amino, N,N-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkylS(O)$_a$, C_{3-6}cycloalkyl, aryl or aryl C_{1-6} alkylS(O)$_a$ wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

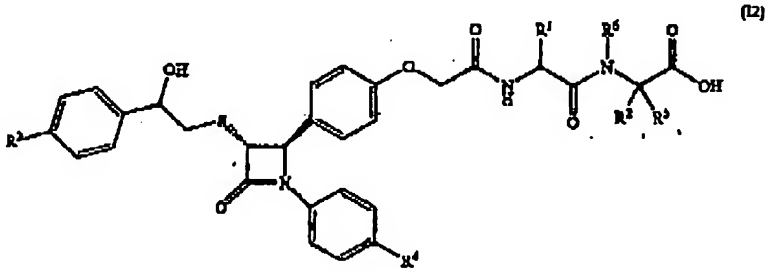
R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylS—;

R^4 is hydrogen, C_{1-6}alkyl, halo or C_{1-6}alkoxy;

R^5 is hydrogen, C_{1-6} alkyl or arylC_{1-6} alkyl;

wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^4 and R^3 may form a ring with 3-6 carbon atoms;

or according to formula (I2)



wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_1alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy C_{1-6}alkoxy, N-(C_{1-6}alkyl)amino, N,N-(C_1-C_6 alkylcarbonylamino, C_{1-6}-alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^2 and R^3 are independently hydrogen, a branched or unbranched C_{1-6}alkyl

C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, (C_1-C_6)$_3$Si, N—(C_{1-6}alkyl)amino, N,N-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkylS(O)$_a$, C_{3-6}cycloalkyl, aryl or aryl C_{1-6} alkylS(O)$_a$, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^4 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylS ;

R^4 is hydrogen, C_{1-6}alkyl, halo or C_{1-6}alkoxy:

R^5 is hydrogen, C_{1-6} alkyl or arylC_{1-6} alkyl

wherein R^3 and R^3 may form a ring with 2-7 carbon atoms and wherein R^4 and R^2 may form a ring with 3-6 carbon atoms;

with a PPAR alpha and/or gamma agonist.

19. A combination of a compound according to formula (I)

wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy C_{1-6}alkoxy, N-(C_{1-6}alkyl)amino, N,N-(C_{1-6} alkylcarbonylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

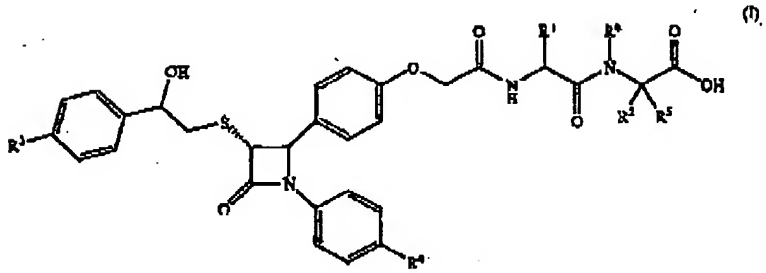
R^2 and R^6 are independently hydrogen, a branched or unbranched C_{1-6}alkyl C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, (C_1-C_6)$_3$Si, N-(C_{1-6}alkyl)amino, N,N-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkylS(O)$_a$, C_{3-6}cycloalkyl, aryl or aryl C_{1-6} alkylS(O)$_a$, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylS ;

R^4 is hydrogen, C_{1-6} alkyl halo or C_{1-6}alkoxy;

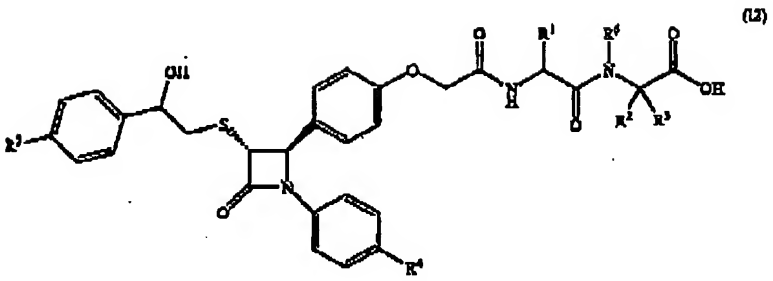
R^6 is hydrogen, C_{1-6} alkyl, or arylC_{1-6} alkyl;

wherein R^3 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;



(I)

or according to formula (12)


(12)

wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy C_{1-6}alkoxy, N—(C_{1-6}alkyl)amino, N,N-(C_{1-6}alkyl)$_2$amino, C_1-C_6alkylcarbonylamino, C_{1-6}alkylS(O)$_n$ wherein n is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^2 and R^3 are independently hydrogen, a branched or unbranched C_{1-6}alkyl C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, (C_1-C_4)$_3$Si, N—(C_{1-6}alkyl)amino, N,N-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkylS(O)$_n$, C_{3-6}cycloalkyl, aryl or aryl C_{1-6} alkylS(O)$_n$ wherein n is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylS -;

R^4 is hydrogen, C_{1-6} alkyl halo or C_{1-6}alkoxy;

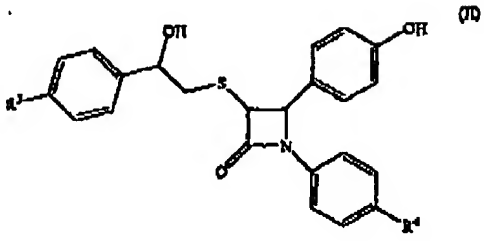
R^5 is hydrogen, C_{1-6} alkyl or arylC_{1-6} alkyl;

wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^5 and R^3 may form a ring with 3-6 carbon atoms;

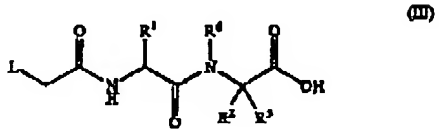
with an HMG Co-A reductase inhibitor.

20. A process for preparing a compound or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof comprising:

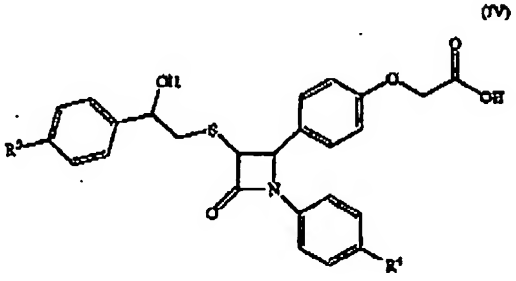
a) reacting a compound of formula (II):


(II)

with a compound of formula (III):

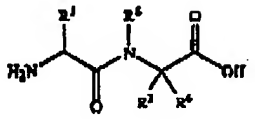

(III)

b) reacting an acid of formula (IV):


(IV)

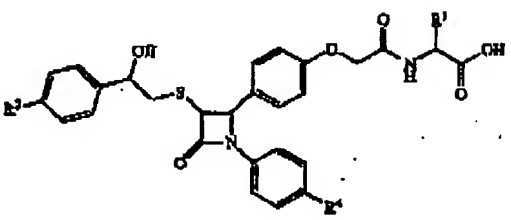
or an activated derivative thereof;

with an amine of formula (V):



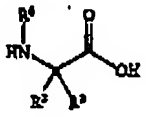
(V)

c) reacting an acid of formula (VI):



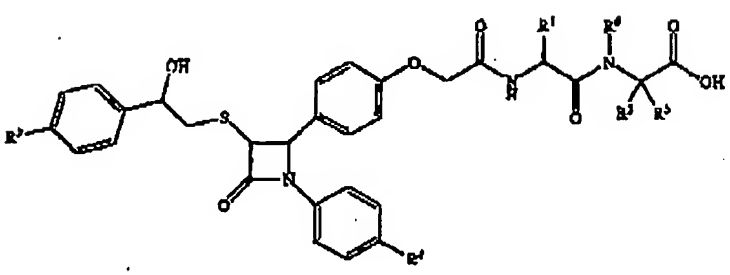
(VI)

or an activated derivative thereof, with an amine of formula (VII):



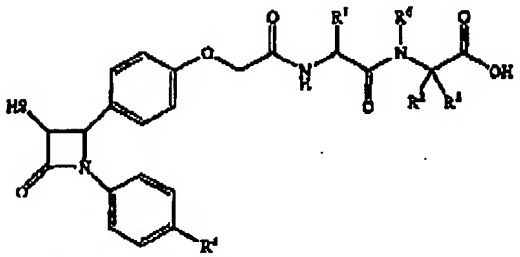
(VII)

d) reducing a compound of formula (VIII):



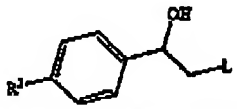
(VIII)

e) reacting a compound of formula (IX):



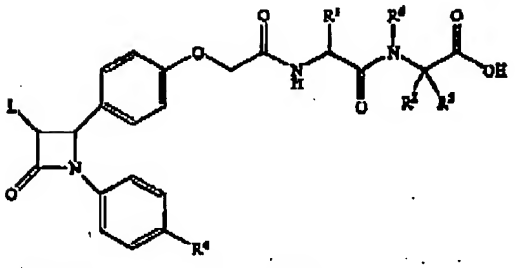
(IX)

with a compound of formula (X):



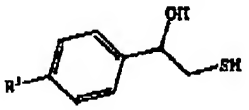
(X)

f) reacting a compound of formula (XI):



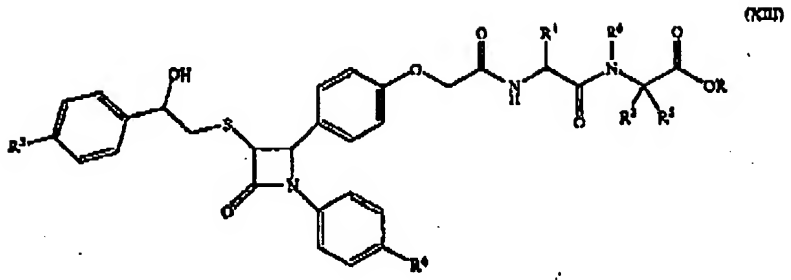
(XI)

with a compound of formula (XII):



(XII)

g) De-esterifying a compound of formula (XIII)



(XIII)

wherein the group C(O)OR is an ester group; and

wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy C_{1-6}alkoxy, N—(C_{1-6}alkyl)amino, N,N-(C_{1-6}alkyl)$_2$amino, C_1-C_6 alkylcarbonylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}-cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^2 and R^3 are independently hydrogen, a branched or unbranched C_{1-6}alkyl C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, (C_1-C_4)$_3$Si, N—(C_{1-6}alkyl)amino, N,N-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkylS(O)$_a$ C_{3-6}cycloalkyl aryl or aryl C_{1-6} alkylS(O)$_a$ wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6} alkyl, or C_{1-6}alkoxy;

R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylS—;

R^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6}alkoxy;

R^5 is hydrogen, C_{1-6} alkyl or arylC_{1-6} alkyl;

wherein R^5 and R^3 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms; and

L is a displaceable group;

and thereafter optionally:

i) converting a compound of the formula (I) into another compound of the formula (I);

ii) removing any protecting groups;

iii) forming a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug; or

iv) separating two or more enantiomers.

21. A method of treating or preventing a hyperlipidemic condition comprising the administration of an effective amount of a compound according to claim 12 to a mammal in need thereof.

22. A method of treating or preventing atherosclerosis comprising the administration of an effective amount of a compound according to claim 12 to a mammal in need thereof.

23. A method for treating or preventing Alzheimers' disease comprising the administration of an effective amount of a compound according to claim 12 to a mammal in need thereof.

24. A method for treating or preventing a cholesterol associated tumor comprising the administration of an effective amount of a compound according to claim 12 to a mammal in need thereof.

25. A pharmaceutical formulation comprising a compound according to claim 12 in admixture with a pharmaceutically acceptable adjuvant, diluent and/or carrier.

26. A process according to claim 20 wherein L is a halogen or sulphonyloxy group.

27. A process according to claim 26 wherein L is a chloro, bromo, methanesulphonyloxy or toluene-4-sulphonyloxy group.

28. A process according to claim 20 wherein the C(O)OR ester group is methoxycarbonyl, ethoxycarbonyl, t-butoxycarbonyl, or benzyloxycarbonyl.

* * * * *

Preliminary Amendment.

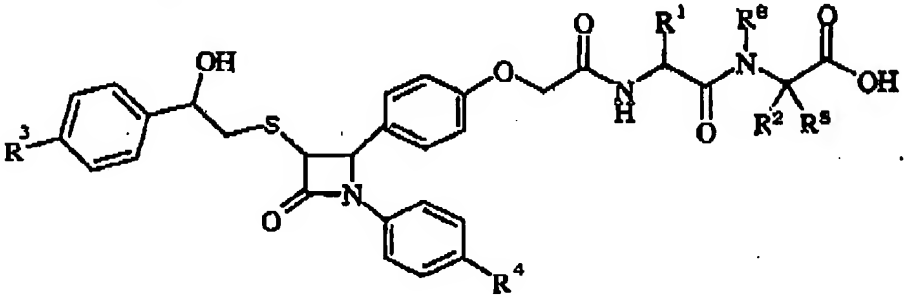
DOCKET NO.: ASZN0107-100 (101340-1P US) **PATENT**

In the Claims:

The current status of all claims is listed below and supercedes all previous lists of claims.

Please amend claims 1-20, and add new claims 21-28 as follows.

1. (currently amended) A compound of formula (I):



(I)

wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6}alkoxy, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, ~~C_1-C_6alkylcarbonylamino~~ C_1-C_6 alkylcarbonylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^2 and R^5 are independently hydrogen, a branched or unbranched C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, $(C_1$-$C_4)_3$Si, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, ~~C_{1-6}alkylS(O)$_a$~~, C_{1-6}alkylS(O)$_a$, C_{3-6}cycloalkyl, aryl or aryl C_{1-6} alkylS(O)$_a$, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylS-;

R^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6}alkoxy;

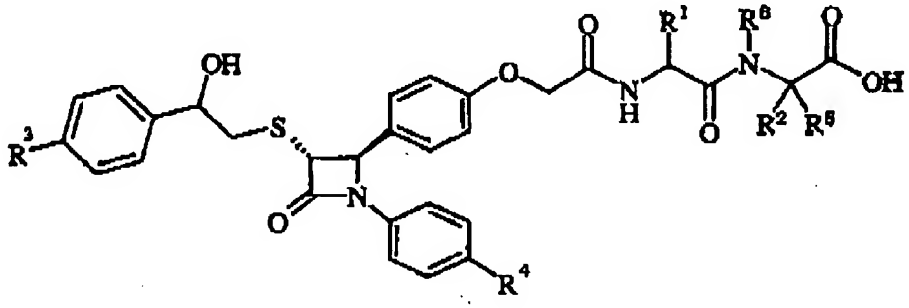
R^6 is hydrogen, C_{1-6} alkyl, or arylC_{1-6} alkyl;

wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(*N*-{*N*-[(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl}carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-{4-[*N*-((R)-α-{*N*-[(S)-1-(carboxy)-2-(hydroxy) ethyl]carbamoyl}benzyl)carbamoylmethoxy]phenyl}azetidin-2-one.

2. (currently amended) A compound of formula (I2):



(I2)

wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6}alkoxy, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, ~~C_1-C_6 alkylcarbonylamino~~ C_1-C_6 alkylcarbonylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^2 and R^5 are independently hydrogen, a branched or unbranched C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, $(C_1$-$C_4)_3$Si, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, ~~C_{1-6}alkylS(O)$_a$~~, C_{1-6}alkylS(O)$_a$, C_{3-6}cycloalkyl, aryl or

aryl C_{1-6} alkylS(O)$_a$, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylS-;

R^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6}alkoxy;

R^6 is hydrogen, C_{1-6} alkyl, or arylC_{1-6} alkyl;

wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(*N*-{*N*-[(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl}carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-{4-[*N*-((R)-α-{*N*-[(S)-1-(carboxy)-2-(hydroxy) ethyl]carbamoyl}benzyl)carbamoylmethoxy]phenyl}azetidin-2-one.

3. (currently amended) A compound according to claim 1 ~~or 2~~, wherein:

R^1 is hydrogen or phenyl.

4. (currently amended) A compound according to ~~any of the preceding claims~~ claim 1, wherein:

R^2 is hydrogen, a branched or unbranched C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, acylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by hydroxy, alkyl, alkoxy or cyano.

5. (currently amended) A compound according to ~~any of the preceding claims~~ claim 1, wherein:

R^3 is hydrogen, C_1-C_2alkyl, halo or methoxy.

6. (currently amended) A compound according to ~~any of the preceding claims~~ claim 1, wherein:

R^3 is hydrogen, methyl, chlorine, fluorine, C_{1-6} alkylS-, or methoxy.

7. (currently amended) A compound according to ~~any of the preceding claims~~ claim 1, wherein:

R^4 is hydrogen or halo.

8. (currently amended) A compound according to ~~any of the preceding claims~~ claim 1, wherein:

R^4 is chlorine or fluorine.

9. (currently amended) A compound according to ~~any of the preceding claims~~ claim 1, wherein:

R^5 is hydrogen, C_{1-6} alkyl, arylC_{1-6}alkyl or R^6 and R^2 form a ring with 3-6 carbon atoms.

10. (currently amended) A compound according to claim 1, wherein:

R^1 is hydrogen;

R^2 is a branched or unbranched C_{1-6}alkyl, optionally substituted by a C_{3-6}cycloalkyl, alkylS-, aryl optionally substituted by hydroxy or cyano, amino, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino or aryl C_{1-6} alkyl*S*(O)$_n$, wherein n is ~~0-2~~ 0-2;

R^3 and R^4 are halo;

R^5 is hydrogen or C_{1-6} alkyl; and

R^6 is hydrogen.

11. (currently amended) One or more compounds chosen from:

N-{[4-((2R,3R)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-N^6-acetyl-D-lysine;

1-(4-Fluorophenyl)-3-(R)-[2-(4-fluorophenyl)-2-hydroxyethylthio]-4-(R)-{4-[*N*-{*N*-[2-

(phenyl)-1-(R)-(carboxy)ethyl]carbamoylmethyl}carbamoylmethoxy]phenyl}azetidin-2-one;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-valine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-tyrosine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-proline;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-lysine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-hydroxy-2-(4-methoxyphenyl)ethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-valine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-2-butylnorleucine;

N-{[4-((2*R*,3*R*)-1-(4-Fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-*S*-methyl-L-cysteine;

N-{[4-((2*R*,3*R*)-1-(4-chlorophenyl)-3-{[2-(4-chlorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-cyclohexyl-D-alanine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-cyclohexyl-D-alanine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-4-methylleucine;

N-{[4-((2*R*,3*R*)-1-(4-Fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}-L-alanyl-D-valine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-hydroxy-2-(4-methylphenyl)ethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-valine;

N-{[4-((2*R*,3*R*)-1-(4-chlorophenyl)-3-{[2-(4-chlorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-valine;

N-{[4-((2*R*,3*R*)-1-(4-chlorophenyl)-3-{[2-(4-chlorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-methyl-D-valine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-

oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-(2-naphthyl)-D-alanine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-methyl-D-valine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-(3*R*,4*S*,5*R*)-3,4,5,6-tetrahydroxy-D-~~norleucine~~ norleucine;

N-{[4-((2*R*,3*R*)-1-(4-Fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-*N*,2-~~dimethylalanine~~ dimethylalanine;

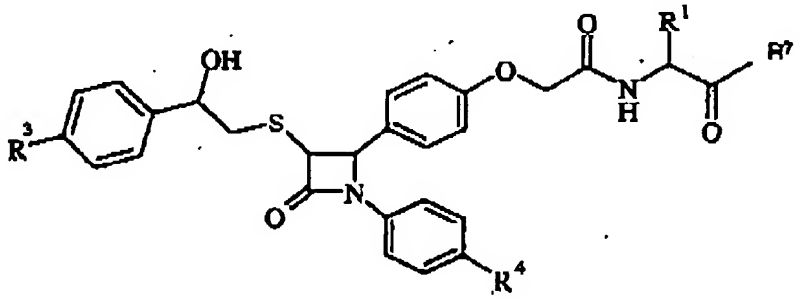
Valine listed 2x → *N*-{[4-[(2*R*,3*R*)-1-(4-Fluorophenyl)-3-({2-hydroxy-2-[4-(methylthio)phenyl]ethyl}thio)-4-oxoazetidin-2-yl]phenoxy}acetyl)glycyl-3-methyl-D-~~valine~~ valine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-*S*-(4-methylbenzyl)-D-~~cysteine~~ cysteine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-*S*-(*tert*-butyl)-D-~~cysteine~~ cysteine; and

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-b,b-dimethyl-D-phenylalanine.

12. (currently amended) A compound of the formula (XV) or hydrolysable esters or amides thereof:



(XV)

wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be

optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6}alkoxy, *N*-(C_{1-6}alkyl)amino, *N*,*N*-(C_{1-6}alkyl)$_2$amino, ~~C_3-C_6alkylcarbonylamino~~ C_1-C_6 alkylcarbonylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^2 and R^5 are independently hydrogen, a branched or unbranched C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, (C_1-C_4)$_3$Si, *N*-(C_{1-6}alkyl)amino, *N*,*N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkylS(O)$_a$, ~~aryl-C_{1-6} alkylS(O)$_a$~~ arylC$_{1-6}$ alkylS(O)$_a$, wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylS-;

R^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6}alkoxy;

R^6 is hydrogen, C_{1-6} alkyl, or arylC$_{1-6}$ alkyl; and

R^7 is an hydroxy group or a C_{1-3} alkoxy group;

wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(*N*-{*N*-[(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl}carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-{4-[*N*-((R)-α-{*N*-[(S)-1-(carboxy)-2-(hydroxy) ethyl]carbamoyl}benzyl)carbamoylmethoxy]phenyl}azetidin-2-one.

13. (currently amended) A method of treating or preventing a hyperlipidemic condition ~~hyperlipidemic conditions~~ comprising the administration of an effective amount of a compound according to ~~any one of claims 1 to 12~~ claim 1 to a mammal in need thereof.

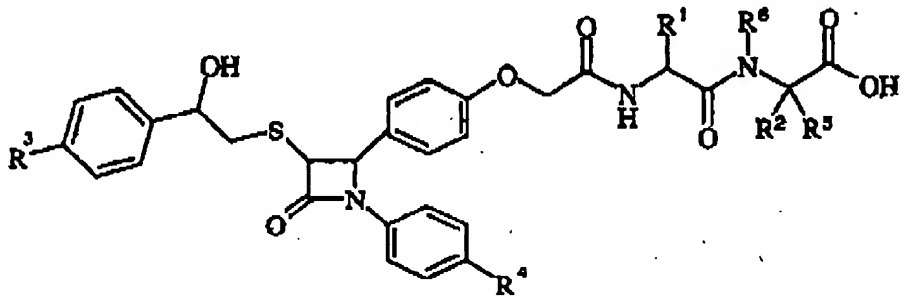
14. (currently amended) A method of treating or preventing atherosclerosis comprising the administration of an effective amount of a compound according to ~~any one of claims 1 to 12~~ claim 1 to a mammal in need thereof.

15. (currently amended) A method for treating or preventing Alzheimers' disease comprising the administration of an effective amount of a compound according to ~~any one of claims 1 to 12~~ claim 1 to a mammal in need thereof.

16. (currently amended) A method for treating or preventing a cholesterol associated tumor ~~cholesterol associated tumors~~ comprising the administration of an effective amount of a compound according to ~~any one of claims 1 to 12~~ claim 1 to a mammal in need thereof.

17. (currently amended) A pharmaceutical formulation comprising a compound according to ~~any one of claims 1 to 12~~ claim 1 in admixture with a pharmaceutically acceptable adjuvant, diluent and/or carrier ~~adjuvants, diluents and/or carriers~~.

18. (currently amended) A combination of a compound according to formula (I)



(I)

wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6}alkoxy, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_1-C_6alkylcarbonylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be

optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^2 and R^5 are independently hydrogen, a branched or unbranched C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, $(C_1-C_4)_3Si$, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkylS(O)$_a$, C_{3-6}cycloalkyl, aryl or aryl C_{1-6} alkylS(O)$_a$, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

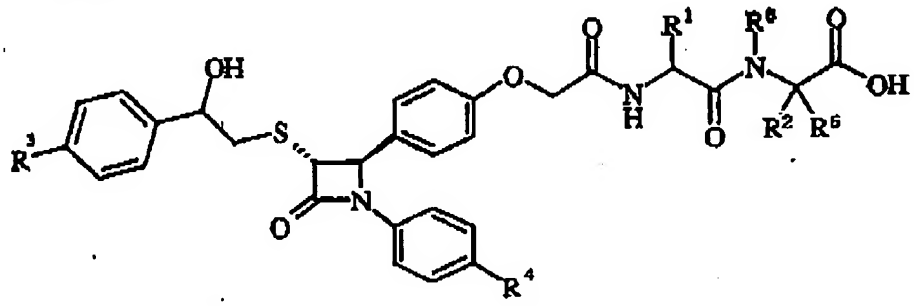
R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylS-;

R^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6}alkoxy;

R^6 is hydrogen, C_{1-6} alkyl, or arylC_{1-6}alkyl;

wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

or according to formula (I2)



(I2)

wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6}alkoxy, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_1-C_6 alkylcarbonylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^2 and R^5 are independently hydrogen, a branched or unbranched C_{1-6}alkyl,

C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, $(C_1-C_4)_2Si$, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkylS(O)$_a$, C_{3-6}cycloalkyl, aryl or aryl C_{1-6} alkylS(O)$_a$, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylS-;

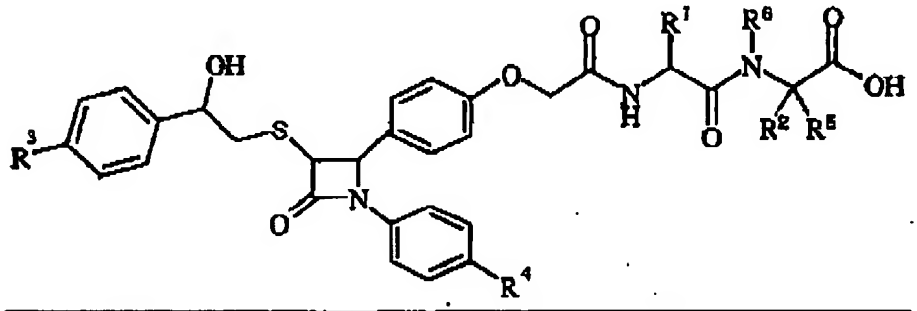
R^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6}alkoxy;

R^6 is hydrogen, C_{1-6} alkyl, or arylC_{1-6} alkyl;

wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

with a PPAR alpha and/or gamma agonist.

19. (currently amended) A combination of a compound according to formula (I)



(I)

wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6}alkoxy, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_1-C_6alkylcarbonylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{3-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^2 and R^5 are independently hydrogen, a branched or unbranched C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more

hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, $(C_1-C_4)_3Si$, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkylS(O)$_a$, C_{3-6}cycloalkyl, aryl or aryl C_{1-6} alkylS(O)$_a$, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

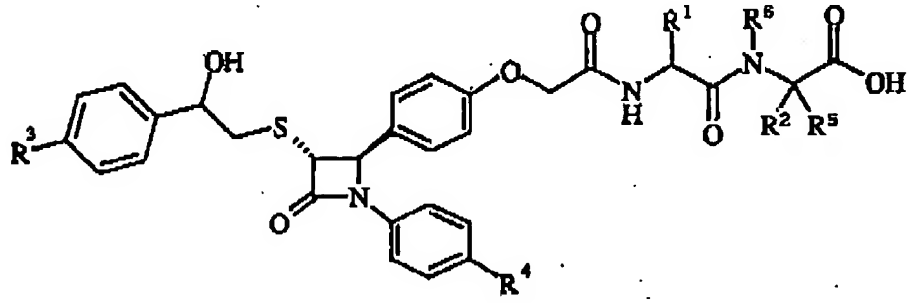
R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylS-;

R^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6}alkoxy;

R^6 is hydrogen, C_{1-6} alkyl, or arylC_{1-6} alkyl;

wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

or according to formula (I2)



(I2)

wherein:

R^1 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6}alkoxy, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_1-C_6 alkylcarbonylamino, C_{1-6}alkylS(O)$_a$ wherein a is 0-2, C_{1-6}cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^2 and R^5 are independently hydrogen, a branched or unbranched C_{1-6}alkyl, C_{3-6}cycloalkyl or aryl; wherein said C_{1-6}alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6}alkoxy, aryl C_{1-6}alkoxy, $(C_1-C_4)_3Si$, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkylS(O)$_a$, C_{3-6}cycloalkyl, aryl or aryl C_{1-6} alkylS(O)$_a$ wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or

two substituents selected from halo, hydroxy, C_{1-6}alkyl or C_{1-6}alkoxy;

R^3 is hydrogen, alkyl, halo, C_{1-6}alkoxy or C_{1-6} alkylS-;

R^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6}alkoxy;

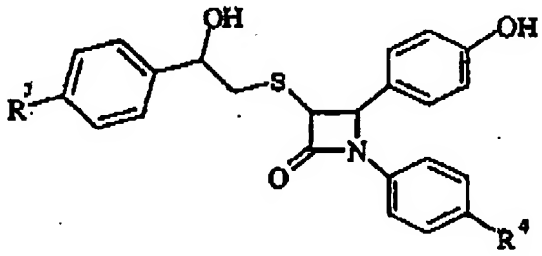
R^6 is hydrogen, C_{1-6} alkyl, or arylC_{1-6} alkyl;

wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

with an HMG Co-A reductase inhibitor.

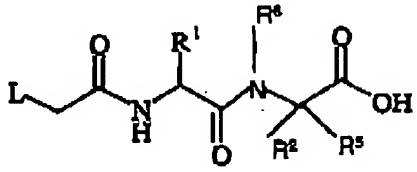
20. (currently amended) A process for preparing a compound ~~of formula (I)~~ or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof ~~which process (wherein variable groups are, unless otherwise specified, as defined in formula (I)) comprises of~~ comprising:

~~*Process 1)*~~ a) reacting a compound of formula (II):



(II)

with a compound of formula (III):



(III)

~~wherein L is a displaceable group;~~

~~*Process 2)*~~ b) reacting an acid of formula (IV):

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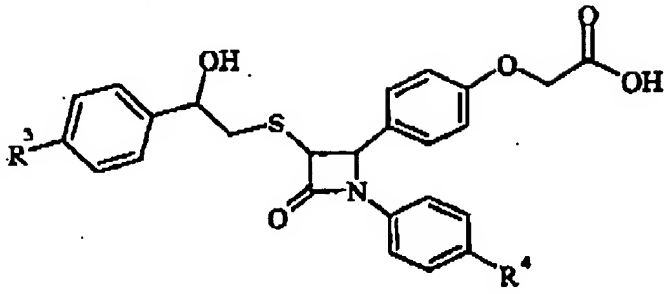
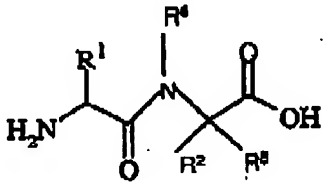


(IV)

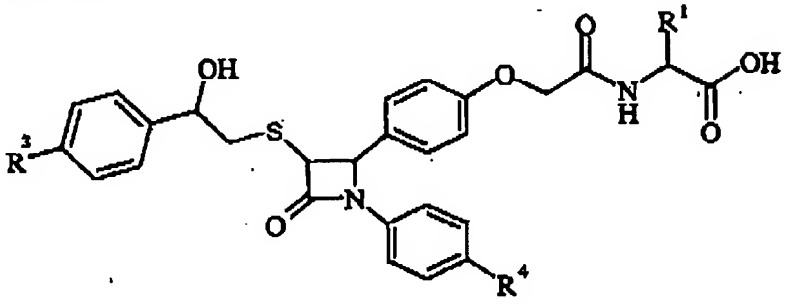
or an activated derivative thereof;

with an amine of formula (V):



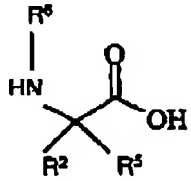
(V)

~~*Process 3):*~~ c) reacting an acid of formula (VI):



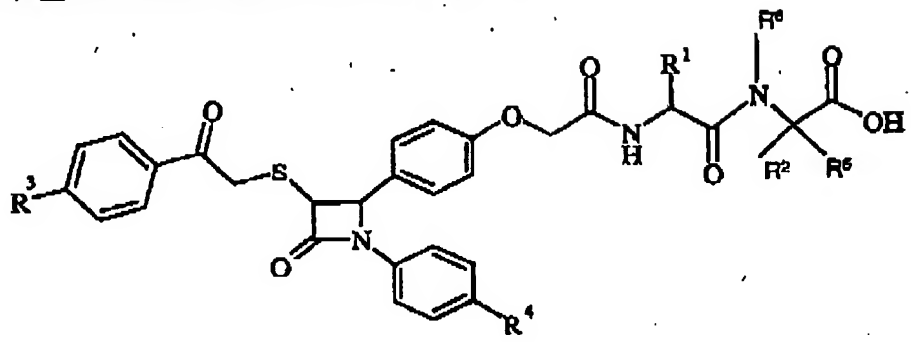
(VI)

or an activated derivative thereof, with an amine of formula (VII):



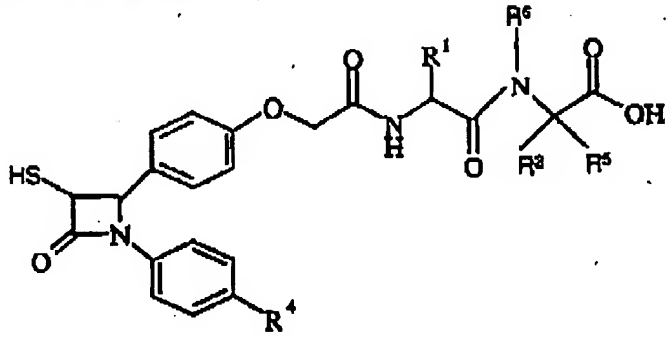
(VII)

~~*Process 4):*~~ d) reducing a compound of formula (VIII):



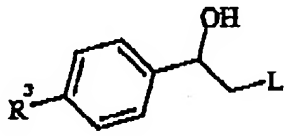
(VIII)

~~*Process 5):*~~ e) reacting a compound of formula (IX):



(IX)

with a compound of formula (X):



(X)

~~wherein L is a displaceable group;~~

~~*Process 6):*~~ f) reacting a compound of formula (XI):